

## REMARKS

Claims 401-414, 416-419 and 421-463 are pending. Claims 402-410, 413, 425-259 and 461 are withdrawn. Claims 415 and 420 are cancelled without prejudice. Applicants reserve the right to pursue the subject matter of these claims in one or more continuing applications. Claims 401, 411, 412, 421, 423, 462 and 463 are amended. No new matter is added.

### **35 U.S.C. § 112, First Paragraph, Rejections - Enablement**

The Examiner has rejected claims 401, 411-412, 414-424, 434, 436-438, 460 and 462 under 35 U.S.C. first paragraph, for alleged lack of enablement. Applicants request clarification with respect to the rejection of claims 434 and 436-438 as Applicants understand that these claims have been withdrawn as noted on page 1 of the Office Action.

While acknowledging that the instant specification is enabling for a method of expanding an *ex-vivo* population of CD34+ and CD34+CD38- hematopoietic stem cells in culture, while at the same time inhibiting differentiation of said cells, utilizing a specific concentration of nicotinamide, nicotinamide analog or nicotinamide derivative, the Examiner asserts that the specification fails to provide enablement for expanding any stem cell with any amount of nicotinamide, nicotinamide analog or nicotinamide derivative. *See*, Office Action at pages 3-8. Applicants traverse the rejection with respect to the pending claims as amended herein.

To support this position, the Examiner has cited several publications, including Yang et al (PNAS 2002, 99:8078), Peled et al. (US Patent Application No: 2005/0054097), Hayek et al (WO 2005/086845), Rankin et al, and Banasik, et al.. Applicants submit that these references do not support the assertion that “the state of prior art discusses that expansion and decreased differentiation of hematopoietic stem cells...occurs, as compared to non-treated cells, by specific concentrations and exposure times to nicotinamide” or the assertion “that incubation of stem cells with nicotinamide preferentially contributes to differentiation or proliferation depending on the type of stem cell. For example, incubation of hepatic oval stem cells with nicotinamide differentiates said stem cells into insulin producing cells.”

However, in order to expedite prosecution, independent claims 401 (from which claims 414, 416-419, 421-424 depend), 411, 412 and 463 are amended to require that the stem cells are “hematopoietic stem cells” and require that the hematopoietic stem cells are cultured or propagated in the presence of “at least 0.1 mM of exogenously added nicotinamide, nicotinamide analog or nicotinamide derivative.” Support for such an amendment can be found throughout the

instant specification, for example, at page 72, lines 3-7, of the instant specification. Methods for expanding “hematopoietic stem cells in the presence of at least 0.1 mM of exogenously added nicotinamide, nicotinamide analog or nicotinamide derivative is well described in Example 5 beginning at page 137.

Applicants also require clarification with respect to the rejection of claim 460 as claim 460 is directed to an ex vivo expanded population of hematopoietic stem cells which comprise CD34+ cells which as stated by the Examiner above are enabled by the instant specification.

In view of the foregoing arguments and amendments, Applicants submit that one of ordinary skill in the art would be able to use the claimed methods, as taught, without undue experimentation. Reconsideration and withdrawal of the instant rejections is therefore respectfully requested.

### **35 U.S.C. § 102(e), First Paragraph, Rejections - Enablement**

The Examiner has rejected claims 401, 411, 412, 414-418, 420-424 and 462 under 35 U.S.C. § 102(e) as being anticipated by US Patent Publication No. 2002/0159984) to Brown (“Brown”). See, Office Action at pages 9-10. Applicants traverse the rejection with respect to the pending claims as amended herein.

As described above, independent claims 401 (from which claims 414, 416-418, 421-424 depend), 411, 412 and 462 are amended to require that the stem cells are “hematopoietic stem cells” and require that the hematopoietic stem cells are cultured or propagated in the presence of “at least 0.1 mM of exogenously added nicotinamide, nicotinamide analog or nicotinamide derivative.”

Brown teaches that nicotinamide is added as standard ingredient of the basic medium, at the single physiological concentration of 4mg/L (see Table I), which is 0.033 mM. As such, Brown does not teach or suggest all the limitations (“at least 0.1 mM”) of the pending claims as amended. Applicants respectfully request reconsideration and withdrawal of the present invention.

### **Double Patenting Rejections**

Claim 411 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claim 208 of co-pending U.S. Application No. 10/767,064. Applicants traverse.

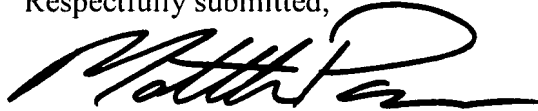
APPLICANTS: Peled et al.  
SERIAL NUMBER: 10/774,843

Claim 208 of co-pending U.S. Application No. 10/767,064 is withdrawn as of the Office Action mailed January 18, 2007. As such, this rejection is moot and should be withdrawn.

### CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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